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Full paper

Dentin hypersensitivity-like tooth pain seen in patients receiving steroid therapy: An exploratory study

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ABSTRACT

To ascertain whether steroid therapy evokes dentin hypersensitivity (DH)-like tooth pain, we performed a study based on compelling evidence from patients receiving steroid therapy. An exploratory study was conducted using a questionnaire for 220 patients prescribed steroids who attended the Department of Hematology and Rheumatology of Tohoku University Hospital. Group comparisons between patients with and without steroid pulse therapy were analysed by statistical means. In this study, any DH-like tooth pain that commenced subsequent to steroid treatment was defined as steroid-derived (SD) tooth pain. The prevalence of SD tooth pain was 17.7% (39/220 patients). SD tooth pain was triggered in many vital teeth by cold and/or hot water (84.2% and 23.7%, respectively) with the pain characterised as continuous, in contrast to typical DH tooth pain. SD tooth pain was significantly more frequent in pulse therapy patients than in non-pulse therapy patients ($p < 0.05$). Logistic regression analysis adjusted for age and sex showed similar results (odds ratio = 3.74, $p = 0.013$). Moreover, a positive correlation was observed between the steroid dose and pain score ($\rho = 0.642$). Dose reduction or discontinuation of steroid therapy relieved SD tooth pain in all cases. Thus, steroid therapy can evoke DH-like tooth pain during treatment.

1. Introduction

Dentin hypersensitivity (DH) is a common oral condition characterised by intense, transient pain induced by stimulation or irritation of exposed dentin, and is generally elicited in response to chemical, cold, tactile, or osmotic stimuli (1). Numerous informal reports on social media (e.g., weblogs, Twitter, and Facebook) have revealed the prevalence of severe DH-like tooth pain in patients taking steroids. Several of these reports have stated that this pain is among the most irritating of steroid-derived side effects, along with having a puffy face caused by water retention. However, DH-like tooth pain is not documented in the academic literature as one of the side effects of steroid therapy, although steroids have many well-known side effects (e.g., lipodystrophy, neuropsychiatric disorders, skin disorders, muscle cramps, and weakness in proximal muscles) (2).

Paradoxically, therapies involving corticosteroids are well known to relieve pain because of their anti-inflammatory and/or anti-oedema effects (3). However, it is unknown whether steroid administration can influence the pain threshold. We recently found that, using a rat model, prednisolone induces microglial activation specifically in the subnucleus caudalis, and not in other nuclei of the trigeminal sensory complex (4), where the primary sensory nerves innervating the pulp project. This finding suggests that steroid therapy may be associated with DH-like tooth pain in patients.

Here, we surveyed patients undergoing steroid therapy in an exploratory study. We used a questionnaire that included items exploring sex, age, primary disease, steroid dose, experience of DH-like tooth pain, and pain characteristics (e.g., triggers and severity)

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to determine the potential relationship between steroid therapy and DH-like tooth pain.

2. Materials and methods

2.1. Study population

The subjects comprised 220 patients (40 males and 180 females) with a mean age of 49.9 years (range: 17–87 years) who attended and received steroid therapy at the Department of Hematology and Rheumatology of Tohoku University Hospital. In this study, a control group of non-steroid subjects was not included because our preliminary survey showed all non-steroid subjects who met the inclusion and exclusion criteria described below did not suffer from DH-like tooth pain. The most common primary diseases for which patients were prescribed steroid therapy were systemic lupus erythematosus (SLE; n = 93), rheumatoid arthritis (RA; n = 70), Sjögren's syndrome (n = 17), Takayasu's arteritis (n = 16), mixed connective tissue disease (n = 9), and dermatomyositis (n = 5). Patients who experienced tooth pain before steroid therapy, dental caries (including wedge-shaped defects), and/or had five or fewer remaining vital teeth were excluded from the study after clinical examination (dental checkup) at the Department of Oral Diagnosis of Tohoku University Hospital. The present study was approved by the Ethics Committee of Tohoku University Graduate School of Dentistry (approval no. 2011/22-31). Written informed consent was obtained from all participants or their guardians (17–19-year-old participants). This survey was conducted following the ethical principles of medical investigation involving human subjects under the Helsinki Declaration of the World Medical Association (http://www.wma.net).

2.2. Study design

An exploratory study using a questionnaire was carried out at Tohoku University Hospital between June 2011 and July 2015. The questionnaire was administered once and patients were asked questions on items such as sex, age, primary disease, treatment received (e.g., steroid therapy and/or steroid pulse therapy), experience of DH-like tooth pain, and pain characteristics (e.g., site, onset, triggers, and the pain severity score expressed on a visual analogue scale [VAS]). Steroid pulse therapy comprised methylprednisolone administration (500–1000 mg/day, i.v.) for 3 days. Non-pulse therapy consisted of prednisolone administration (1–200 mg/day, p.o.). We compared the maximum pain sensation (VAS based on patient recall) with the present maximum pain sensation (VAS described at that time). Steroid doses at these time points were determined using the patients' medical charts. Changes in the pain score were compared before and after reduction or discontinuation of the steroid. For the purposes of this study, any DH-like tooth pain that commenced subsequent to taking steroids was defined as 'steroid-derived (SD) tooth pain' after a dental checkup according to the inclusion and exclusion criteria described above. We also examined the effects of dental treatments generally provided for DH, which were delivered upon patient request for alleviation of SD tooth pain. These DH treatments included application of MS Coat ONE (Sun Medical Co., Ltd., Moriyama, Japan), Teethmate Desensitizer (Kuraray Noritake Dental Inc., Tokyo, Japan), and Saforide (Bee Brand Medico Dental Co., Ltd., Osaka, Japan).

2.3. Statistical analysis

The chi-squared test was used for comparison of qualitative data. Fisher's exact test was used for comparison of steroid pulse therapy and presence of tooth pain because of the small expected value. Logistic regression analysis was then applied to estimate the odds ratio (OR) of steroid pulse therapy for presence of tooth pain adjusting for age and sex. To consider the effect of diseases on tooth pain, the presence of SLE, RA, and other diseases was added to the model.

The relationship between steroid dose and pain sensation evaluated by the VAS was analysed by calculating the correlation coefficient (ρ). Significant differences in tooth pain as quantified by the VAS at the maximum steroid dose and after discontinuation or dose reduction were determined using the paired t-test. Statistical analyses were performed using PASW statistics, v18.0 (SPSS Inc., Chicago, IL, USA). Logistic regression analyses were conducted using STATA SE version 14.1 (Stata Corp, College Station, TX, USA). Differences were considered significant at $p < 0.05$.

3. Results

3.1. Prevalence of SD tooth pain in patients receiving pulsed and non-pulsed steroid therapy

As shown in Table 1, the prevalence of SD tooth pain in patients taking steroids was 17.7% (39/220 patients). There were no significant differences in the prevalence between sex ($p = 0.7135$) or amongst patients with SLE (n = 93), RA (n = 70), or other diseases (n = 97) as the primary disease ($p = 0.4374$). Thirty-six patients had more than one primary disease. The prevalence of SD tooth pain was significantly more frequent in patients treated with steroid pulse therapy (41.2%; 7/17 patients) than in those receiving non-pulse therapy (15.8%; 32/203 patients; $p < 0.05$) (Fig. 1).

Table 2 shows the results of logistic regression analysis. After adjusting for age and sex, logistic regression analysis showed that steroid pulse therapy was significantly associated with SD tooth pain (OR = 3.74, $p = 0.013$). Steroid pulse therapy remained significantly associated with SD tooth pain after considering the effects of diseases (OR = 3.34, $p = 0.029$), indicating that the effect of diseases on SD tooth pain was small.

3.2. Relationship between prednisolone dose and pain severity and the effect of steroid discontinuation or dose reduction on SD tooth pain

A positive correlation between steroid dose (prednisolone) and pain score was observed ($\rho = 0.642$) (Fig. 2). The highest pain score

Table 1
Distribution of patients with steroid treatment (n = 220).

Variables		N (%)
Pain	(−)	181 (82.27)
	(+)	39 (17.73)
Pulse	(−)	203 (92.27)
	(+)	17 (7.73)
Age	40>	69 (31.36)
	40–59	79 (35.91)
	59<	72 (32.73)
Sex	Men	40 (18.18)
	Women	180 (81.82)
SLE	(−)	127 (57.73)
	(+)	93 (42.27)
RA	(−)	150 (68.18)
	(+)	70 (31.82)
Other diseases	(−)	121 (55.00)
	(+)	99 (45.00)

SLE, systemic lupus erythematosus; RA, rheumatoid arthritis; 'Other diseases' include Sjögren's syndrome, Takayasu's arteritis, mixed connective-tissue disease, and dermatomyositis.